

WE CLAIM:

1. A method for determining the genotype of a patient at the SLC6A3 Exon 9 locus, comprising:

determining for the two copies of the SLC6A3 gene present in the patient's blood or tissue, the identity of the nucleotide pair at the polymorphic site in SLC6A3 Exon 9 A59G at position 41370 in GenBank Sequence Accession Reference No.

AF119117.1, and, optionally, classifying the patient as either AA, AG or GG, wherein

- (i) if both nucleotide pairs are AT then the patient is classed as AA;
- (ii) if one nucleotide pair is AT and one is GC then the patient is classed as AG; and
- (iii) if both nucleotide pairs are GC then the patient is classed as GG.

2. A method of predicting the likelihood of suicidal or self destructive behavior or a Type 1 event occurring during treatment of a patient, who is or may be at risk for the occurrence of suicidal or self destructive behavior or a Type 1 event, comprising, making the genotype determination of claim 1, wherein,

- (a) if said patient is classed as AA then they will be considered to be in risk Category I, and
- (b) if said patient is classed as GC then they will be considered to be in risk Category II, and,
- (c) if said patient is classed as GG then they will be considered to be in risk Category III

3. A method of predicting the likelihood of suicidal or self destructive behavior or a Type 1 event occurring during treatment of a patient, who is or may be at risk for the occurrence of suicidal or self destructive behavior or a Type 1 event, comprising, making the determination whether or not a surrogate marker for the SLC6A3 Exon 9 A59G polymorphism is present in the said patient, wherein,

- (a) if said surrogate marker indicates that said patient should be classed as AA then they will be considered to be in risk Category I, and

(b) if said surrogate marker indicates that said patient should be classed as GC then they will be considered to be in risk Category II, and

(c) if said surrogate marker indicates that said patient should be classed as GG then they will be considered to be in risk Category III

4. A method of treatment wherein if the patient is placed in risk Category II or III, as per Claim 2 or 3, then extra suicide/self-destructive behavior precautions are taken during treatment.

5. A method of treatment of a patient, in need of such treatment, wherein if the said patient is placed in Category II or III, as per Claim 2 or 3, and the patient is in need of an anti-psychotic medication then clozapine is chosen to use alone or in combination with other medications, including, but not limited to, other typical or atypical anti-psychotic medications.

6. A method of predicting the likelihood of suicidal or self destructive behavior or a Type 1 event occurring during treatment of a patient, who is or may be at risk for the occurrence of suicidal or self destructive behavior or a Type 1 event, in a patient receiving treatment, comprising:

(a) assaying for the presence and concentration of SLC6A3 polypeptide gene, expression product in the said patient's body fluids or tissues;

(b) determining from the presence and concentration of SLC6A3 polypeptide gene expression product present in said patient's body fluids or tissues whether or not the individual's SLC6A3 genome contains the Exon 9 A59G polymorphism; and

(c) if the presence and concentration of SLC6A3 polypeptide gene expression product indicates the presence of the SLC6A3 genome containing the Exon 9 A59G polymorphism, then said patient is classified into risk Category II or III.

7. A method of treating a patient in need of such treatment, comprising, making the determination described in Claim 6 and if said patient is classified into Category II or III, then extra suicide/self-destructive behavior precautions are taken during the said patient's treatment.

8. A method to treat a patient, in need of such treatment comprising:

- (a) assaying for the presence and concentration of SLC6A3 polypeptide gene expression product in said patient's body fluids or tissues;
  - (b) determining from the SLC6A3 polypeptide gene expression products presence and concentration in said patient's body fluids or tissues, if the said patient's SLC6A3 genome does or does not contain the Exon 9 A59G polymorphism; and
  - (c) wherein if the determination in (b) is that the said patient has a SLC6A3 genome containing the Exon 9 A59G polymorphism then the said patient is classified into risk Category II or III and if the said patient is in need of an anti-psychotic medication then clozapine is chosen to use alone or in combination with other medications including, but not limited to, other typical or atypical anti-psychotic medications.
9. A method of predicting the likelihood of suicidal or self destructive behavior or a Type 1 event occurring during treatment of a patient, who is or may be at risk for the occurrence of suicidal or self destructive behavior or a Type 1 event, comprising:
- (a) detecting a level of mRNA expression corresponding to the G variant of the SLC6A3 gene at the polymorphic site Exon 9 A59G at position 41370 in GenBank Sequence Accession Reference No. AF119117.1;
  - (b) detecting a level of mRNA expression corresponding to the A variant of the SLC6A3 gene at the polymorphic site Exon 9 A59G at position 41370 in GenBank Sequence Accession Reference No. AF119117.1; and
  - (c) comparing the levels of mRNA detected in (a) and (b) above, wherein
    - (i) if (a) is not detected, then the said patient is classified into risk Category I; and
    - (ii) if (a) and (b) are both detected then the said patient is classified into risk Category II; and
    - (iii) if (a) is detected and (b) is not detected then said patient is classified into high risk Category III.
10. A method of treatment of a patient in need of such treatment comprising:
- (a) determining said patient's risk category as in Claim 9; and
  - (b) if the said patient's Category is II or III then extra suicide/self-destructive behavior precautions are taken during treatment.

11. A method of treatment of a patient in need of such treatment comprising:
  - (a) determining said patient's risk category as in Claim 9; and
  - (b) if the category is II or III and if said patient is in need of an anti-psychotic medication then clozapine is chosen to use alone or in combination with other medications including, but not limited to, other typical or atypical anti-psychotic medications.
12. A kit for use in determining treatment strategy for a patient who may be in need of treatment for suicidal or self-destructive behavior comprising:
  - (a) an imaging radioligand able to determine in a PET scan the level of DATBP to determine if said patient's SLC6A3 gene does or does not contain the Exon 9 A59G polymorphism;
  - (b) a container suitable for containing the said imaging radioligand and a sample of body fluid from the said patient;
  - (c) means to determine the presence or absence of the Exon 9 A59G polymorphism of the SLC6A3 gene; and
  - (d) instructions for use of kit including special treatment needs, such as specific medication or levels of observation based on the determination made in (c).
13. A kit for use in determining treatment strategy for a patient who may be in need of treatment for suicidal or self-destructive behavior comprising:
  - (a) a polynucleotide able to recognize and bind to the mRNA expression product of the SLC6A3 gene containing the Exon 9 A59G polymorphism;
  - (b) a container suitable for containing the said polynucleotide and a sample of tissue or body fluid from the said patient wherein the said polynucleotide can contact the SLC6A3 mRNA, if it is present;
  - (c) means to detect the combination of the said polynucleotide with the SLC6A3 mRNA; and
  - (d) instructions for use of kit including special treatment needs, such as specific medication or levels of observation based on the detection made in (c) and the determination of category of risk based on the detection made in (c).

14. A kit for use in determining treatment strategy for a patient who may be in need of treatment for suicidal or self-destructive behavior comprising:
  - (a) a polynucleotide able to recognize and bind to some portion of the DNA sequence of the SLC6A3 gene containing the Exon 9 A59G polymorphism;
  - (b) a container suitable for containing the said polynucleotide and a sample of body fluid or tissue from the said patient wherein the polynucleotide can contact the SLC6A3 DNA sequence if it is present;
  - (c) means to detect the combination of the said polynucleotide with the SLC6A3 DNA sequence; and
  - (d) instructions for use of kit special treatment needs, such as specific medication or levels of observation based on the detection made in (c) and the determination of category of risk based on the detection made in (c).
15. A kit for the identification of a patient's polymorphism pattern at the SLC6A3 polymorphic site, said kit comprising a means for determining a genetic polymorphism pattern at the SLC6A3 polymorphic site at Exon 9 A59G polymorphism site
16. A kit according to Claim 15, further comprising a DNA sample collecting means.
17. A kit according to Claim 15 or 16, wherein the means for determining a genetic polymorphism pattern at the SLC6A3 polymorphic site at Exon 9 A59G polymorphism site comprises at least one SLC6A3 genotyping oligonucleotides.
18. A kit according to any of Claims 15-17, wherein the means for determining a genetic polymorphism pattern at the SLC6A3 polymorphic site at the Exon 9 A59G polymorphism site comprises two SLC6A3 genotyping oligonucleotide.
19. A kit according to any of Claims 15-18, wherein the means for determining a genetic polymorphism pattern at the SLC6A3 polymorphic site at the Exon 9 A59G site comprises at least one SLC6A3 genotyping primer composition comprising at least one SLC6A3 genotyping oligonucleotide.

20. A kit according to Claim 19, wherein the SLC6A3 genotyping primer composition comprises at least two sets of allele specific primer pairs.
21. A kit according to any of Claims 18-20, wherein the two SLC6A3 genotyping oligonucleotides are packaged in separate containers.
22. A method according to any of Claims 1, or 2., wherein the determination step further comprises the use of a kit according to any of Claims 15-21.
23. A kit for the identification of mRNA expression of the SLC6A3 gene, said kit comprising a means for determining the mRNA product of the SLC6A3 gene.
24. A kit according to Claim 23, wherein the means for determining the mRNA product of the SLC6A3 gene comprises a polynucleotide capable of binding to the mRNA expression product of the SLC6A3 gene.
25. A kit according to Claim 23 or 24, wherein the means for determining the mRNA product of the SLC6A3 gene comprises at least one polynucleotide specific for one of the variants of the SLC6A3 gene at the polymorphic site at Exon 9 A59G.
26. A kit according to Claim 25, wherein the polynucleotide is specific for mRNA expression of the G variant of the SLC6A3 gene at the polymorphic site at Exon 9 A59G.
27. A kit according to Claim 25, wherein the polynucleotide is specific for mRNA expression of the A variant of the SLC6A3 gene at the polymorphic site at Exon 9 A59G.
28. A kit according to any of Claims 25, 26 or 27, wherein the polynucleotide is binding the mRNA expression of the G or A variant at Exon 9 A59G of the SLC6A3 gene under stringent hybridization conditions.
29. A kit according to Claim 28, wherein the means for determining the mRNA product of the SLC6A3 gene comprises at least two polynucleotides, wherein one polynucleotide is specific for mRNA expression of the G variant of the SLC6A3 gene at the polymorphic site at

Exon 9 A59G, and the other polynucleotide is specific for mRNA expression of the A variant of the SLC6A3 gene at the polymorphic site at Exon 9 A59G.

30. A kit according to Claim 29, wherein the two polynucleotides are packaged in separate containers.

31. A method according to Claim 6, wherein at least one of the determination steps (a) or (b) further comprises the use of a kit according to any of Claims 25-30.

32. A kit for the identification of a patient's SLC6A3 gene polypeptide expression product comprising a means for detecting an imaging radioligand able to determine in a PET scan the level of DATBP to determine if the said patient's SLC6A3 gene does or does not contain the Exon 9 A59G polymorphism.

33. A kit according to Claim 32, wherein the means comprises use of [C]RTI-32 PET imaging radioligand.

34. A kit according to Claim 33, wherein the means comprises use of  $\beta$ -CIT SPECT techniques.

35. A method according to Claim 6, wherein the assaying step (a) comprises the use of a kit according to any of Claims 32-34.

36. A kit according to any of Claims 12-21, 23-30 or 32-35, further comprising a means for collecting a body fluid sample.

37. A method according to any of Claims 1-3, 6, or 9, wherein said method is performed *ex vivo*.

38. A kit, according to any of Claims 12-21, 23-30, or 32-36, wherein the marker being detected is a surrogate marker for the SLC6A3 Exon 9 A59G polymorphism.

39. The method of claim 1 further comprising obtaining a sample of body fluids or other tissue from the patient.

40. An allele-specific nucleic acid probe comprising the nucleic acid sequence of a region of a human SLC6A3 gene or its ribonucleotide equivalent, wherein said region comprises the polymorphic site in SLC6A3 Exon 9 at position 41370.

41. The probe of claim 40 wherein said region contains the A to G transversion at position 41370 (polymorphic site 59 on Exon 9 of the human SLC6A3 gene).